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(54) Process for producing an optically active ruthenium-phosphine complex and process for producing an optically active alcohol by using the complex

Verfahren zur Herstellung von optisch aktiven Rutheniumphosphinkomplexen und deren Verwendung in der Herstellung von optisch aktiven Alkoholen

Procédé pour la production de complexes de ruthénium-phosphine optiquement actifs, et leur utilisation dans la synthèse d'alcools optiquement actifs

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Description

FIELD OF THE INVENTION

1. Field of the Invention

[0001] The present invention relates to a process of reacting a racemic ruthenium phosphine complex with 1/2 equivalent of an optically active diamine having chiral asymmetric activity, thereby inactivating one of the enantiomers, adding an optically active diamine derivative to the other portion of the optically active ruthenium-phosphine complex and thus preparing a ruthenium complex having an optically active diphosphine and an optically active diamine derivative coordinated therein; and a process for preparing an optically active alcohol by making use of the complex.

2. Description of the Related Art

[0002] It is known that a complex formed of a transition metal atom and an organic ligand is used as an asymmetric reaction catalyst. It is also known that an optically active compound, particularly an axially asymmetric diphosphine ligand compound, is selected as the organic ligand. The axially asymmetric diphosphine ligand compound tends to be very expensive and is therefore disadvantageous for industrial use.

[0003] Use of a racemic catalyst, if possible, will be advantageous for the preparation of an inexpensive optically active compound. Two methods are reported for asymmetric synthesis in the presence of a racemic catalyst, that is, (1) a method making use of an asymmetric inactivating agent and (2) a method making use of an asymmetric activating agent.

(1) In "asymmetric inactivating method" which is also called as "chiral poisoning", one of the enantiomers of a racemic catalyst is subjected to selective complex formation/inactivation and reaction is conducted in the presence of the other enantiomer catalyst. For asymmetric inactivation, enantioselective complex formation is an absolute requirement.

[0004] Several reports have so far been made on asymmetric synthesis by using an asymmetric ligand or a metal complex in the racemic form. For example, there is a report in J.M. Brown, et al., *J. Chem. Soc., Chem. Commun.*, 1532 (1986) that an optically pure iridium complex in the (S)-form is allowed to act on CHIRAPHOS (2,3-bisdiphenylphosphinobutane) in the racemic form to form a complex with CHIRAPHOS in the (R)-form and then, the remaining CHIRAPHOS in the (S)-form is made use of as a rhodium complex for asymmetric hydrogenation reaction of dehydroamino acid. It is also reported that a chiral ketone is added to a racemic binaphthol-aluminum complex to inactivate the binaphthol-aluminum complex in the (R)-form by forming a complex therewith and then the remaining binaphthol-aluminium complex in the (S)-form takes part in asymmetric Diels-Alder reaction (H. Yamamoto et al., *J. Am. Chem. Soc.*, 111, 789(1989)), or that a methionine-derived phosphine ligand is added as an inactivating agent to a racemic rhodium complex to inactivate one of the enantiomers thereof, whereby asymmetric hydrogenation of dehydroamino acid is conducted (J. W. Faller et al., *J. Am. Chem. Soc.*, 115, 804(1993)).

[0005] In the above-described three examples, an enantio-selectivity is not so high, suggesting that an inactivated enantiomer complex is not selectively formed.

(2) "Asymmetric activation" of a racemic catalyst means that an asymmetric activating agent forms a complex selectively with one of the enantiomers of the racemic catalyst, thereby imparting it with higher catalytic activity than that of the catalyst before reaction and in the presence of this catalyst imparted with a higher catalytic activity, catalytic asymmetric synthesis is conducted. Even if an enantioselective complex cannot be formed, there is a diastereiomer relationship between two complexes thus formed, for example, (S)-catalyst/(S)-activating agent and (R)-catalyst/(S)-activating agent so that they must be different each other in catalytic activity. If the difference is large, a high enantio-selectivity can be attained. Mikami, who is one of the present inventors, and et al., reported catalytic asymmetric hydrogenation which is effected by asymmetric activation and can permit attainment of a high enantio-selectivity even in the presence of a racemic BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl)-Ru catalyst (T. Ohkuma et al., *J. Am. Chem. Soc.*, 120, 1086(1998)). In this hydrogenation reaction, the asymmetric activating agent forms a complex with each of the enantiomers of the racemic catalyst, thereby forming two activated diastereomer complexes. These two activated complexes in a diastereomeric relation differ largely in catalytic activity and a high enantio-selectivity can be attained, which however depends on the ketone substrate. This method is however accompanied with the problems that a high enantio-selectivity cannot be attained without a large difference between two activated complexes in catalytic activity; and the difference between two activated complexes in catalytic activity depends largely on the ketone substrate to be employed, meaning that the ketone substrate is not generally used.

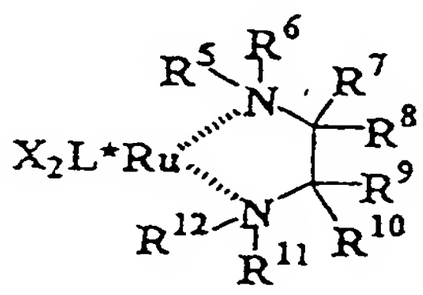
SUMMARY OF THE INVENTION

[0006] The present inventors considered that a more efficient racemic catalyst reaction system can be provided by using two methods for a racemic catalyst, that is, asymmetric activation and asymmetric inactivation in combination and making synergistic use of their merits rather than by using them independently. Described specifically, they considered that if it is possible to inactivate only one of the enantiomers of a racemic catalyst, thereby obtaining only an activated diastereomer complex composed of the other enantiomer, the asymmetric activating method of a racemic BINAP-Ru catalyst improves an enantio-selectivity further and enlarge the application range of its ketone substrate.

[0007] With a view toward overcoming the above-described problems, the present inventors have carried out an extensive investigation. As a result, it has been found that an enantio-selectivity as high as that obtained by asymmetric activation of an optically pure catalyst can be attained by an optically active ruthenium-phosphine complex obtained by subjecting one of the enantiomers of a racemic BINAP-Ru complex to complexation and inactivation by using an inactivating agent and then, adding an asymmetric activating agent to form a complex with the other enantiomer; and that in the presence of the above-described complex, hydrogenation reaction of a carbonyl compound proceeds whereby an optically active alcohol is available at a high optical purity and high yield, leading to the completion of the invention.

[0008] The following are the aspects of the invention.

1) A process for producing a mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex represented by the formula (1):



(1)

wherein R^5, R^6, R^{11} and R^{12} each independently represent a hydrogen atom, a saturated or unsaturated hydrocarbon group, an aryl group, a urethane group or a sulfonyl group; R^7, R^8, R^9 and R^{10} are the same or different so that the carbon to which these substituents have been bonded becomes an asymmetric center and each independently represent a hydrogen atom, an alkyl group, an aromatic monocyclic or polycyclic group, a saturated or unsaturated hydrocarbon group or a cyclic hydrocarbon group; or R^7 or R^8 and R^9 or R^{10} may be coupled together to form an alicyclic group so that the carbon bonded thereto becomes an asymmetric center; L represents a bidentate ligand compound of a tertiary phosphine; X represents a halogen atom; and * means chiral center (L* is an optically active substance); the process comprising the steps of:

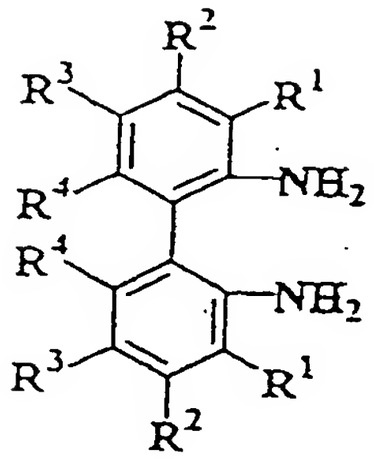
- reacting a ruthenium-phosphine complex represented by the formula (2):

$$Ru_mX_nL_pA_q \qquad (2)$$

wherein X and L have the same meanings as defined above (L is a racemic modification); A represents triethylamine (Et_3N) or dimethylformamide (DMF); and m, n, p and q each stand for an integer and when A represents Et_3N, m, n, p and q stand for 2, 4, 2 and 1, respectively, and when A represents DMF, m, n, p and q stand for 1, 2, 1 and 2 to 5, respectively; or
a ruthenium-phosphine complex represented by the formula (3):

$$[RuX(D)(L)]X \qquad (3)$$

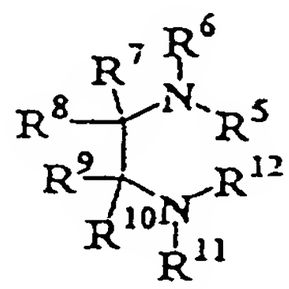
wherein X and L have the same meanings as defined above (L is a racemic modification) and D represents benzene, p-cymene, 1,3,5-trimethylbenzene or hexamethylbenzene;
with ½ equivalent of an optically active chiral diamine represented by the formula (4):



(4)

wherein R^1 represents a C_{1-4} lower alkyl group; R^2 represents a hydrogen atom, a methyl group or a methoxy group; R^3 represents a hydrogen atom, a methyl group, a methoxy group or a chlorine atom; R^4 represents a methyl group, a methoxy group or a trifluoromethyl group; or R^3 and R^4 may be coupled together to form a cyclo ring;
thereby inactivating only one of the enantiomers;
whereby there are obtained the inactivated enantiomer and the other enantiomer, and then

- reacting the other enantiomer with an optically active diamine derivative represented by the formula (5):

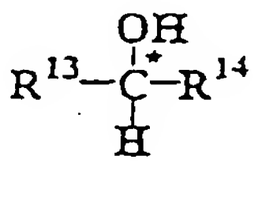


(5)

wherein R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} and R^{12} have the same meanings as defined above;
thereby activating the other enantiomer;
whereby there are obtained the inactivated enantiomer and the activated enantiomer.

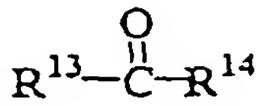
2) A mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex obtainable by the above process.

3) A process for producing an optically active alcohol represented by the following formula (7):



(7)

wherein * means chiral center, R^{13} represents a substituted or unsubstituted monocylic or polycyclic aromatic hydrocarbon group or an α,β-unsaturated C_{2-10} alkyl group and R^{14} represents a substituted or unsubstituted, saturated or unsaturated C_{1-10} hydrocarbon group or a substituted or unsubstituted monocyclic or polycyclic aromatic hydrocarbon group, or R^{13} and R^{14} may be coupled together to form a saturated or unsaturated alicyclic group which may have a substituent for providing a cyclic ketone,
which comprises subjecting, in the presence of a mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex as described above in 1) as a catalyst and a base, a ketone compound represented by the following formula (6):

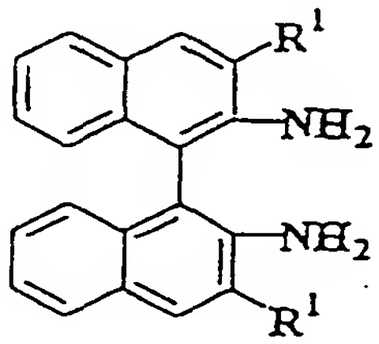


(6)

wherein R^{13} and R^{14} have the same meanings as described above,
to asymmetric hydrogenation.

4) A process for producing an optically active alcohol compound as described above in 3), wherein the base is an alkali metal compound or an alkali earth metal compound.

5) Use of a binaphthyldiamine derivative represented by the formula (4'):



(4')

wherein R^1 represents a C_{1-4} lower alkyl group;
in the process for producing a mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex according to the first aspect.

DETAILED DESCRIPTION OF THE INVENTION

[0009] The invention will next be described more specifically.

[0010] As a ruthenium-phosphine complex to be used in the invention, a ruthenium-phosphine complex represented by the following formula (2):

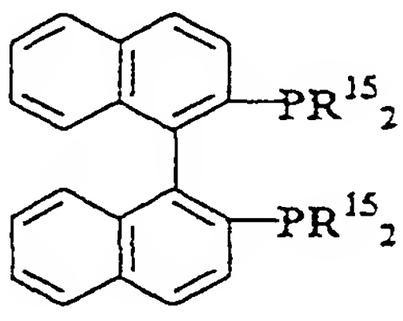
$$Ru_mX_nL_pA_q \qquad (2)$$

wherein X represents a halogen atom; L represents a bidentate ligand compound of a tertiary phosphine (L is a racemic modification) ; A represents triethylamine (Et_3N) or dimethylformamide (DMF); and m, n, p and q each stands for an integer and when A represents Et_3N, m, n, p and q stand for 2, 4, 2 and 1, respectively, and when A represents DMF, m, n, p and q stand for 1, 2, 1 and 2 to 5, respectively; or a ruthenium phosphine complex represented by the following formula (3):

$$[RuX(D)(L)]X \qquad (3)$$

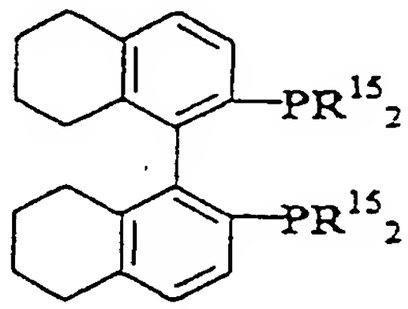
wherein X represents a halogen atom, L represents a bidentate ligand compound of a tertiary phosphine (L is a racemic modification); and D represents benzene, p-cymene, 1,3,5-trimethylbenzene or hexamethylbenzene.

[0011] Specific examples of the L which is a tertiary phosphine include phosphine compounds represented by the following formula (8):



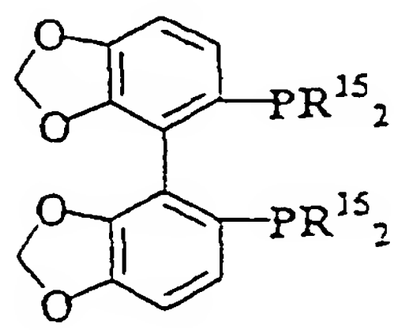
(8)

wherein, R^{15} represents a phenyl, 4-methylphenyl, 3-methylphenyl, 3,5-dimethylphenyl, 4-methoxyphenyl, cyclohexyl or cyclopentyl group (JP-A-3-20290 (the term "JP-A" as used herein means an "unexamined published Japanese patent application) , JP-3-255090, JP-4-74192). Examples of the tertiary phosphine include, in addition to those of the formula (8), those represented by the formula (9):



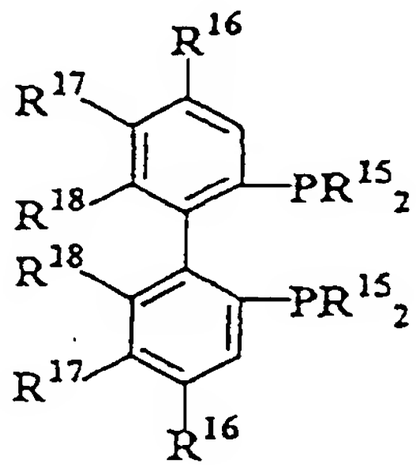
(9)

wherein R^{15} represents a phenyl, 4-methylphenyl, 3-methylphenyl, 3,5-dimethylphenyl, 4-methoxyphenyl, cyclohexyl or cyclopentyl group (JP-4-139140). Examples of the tertiary phosphine include, in addition to the above-exemplified ones, those represented by the formula (10):



(10)

wherein R^{15} represents a phenyl, 4-methylphenyl, 3-methylphenyl, 3,5-dimethylphenyl, 4-methoxyphenyl, cyclohexyl or cyclopentyl group (JP-10-182678). Examples of the tertiary phosphine include, in addition to the above-exemplified ones, those represented by the formula (11) :



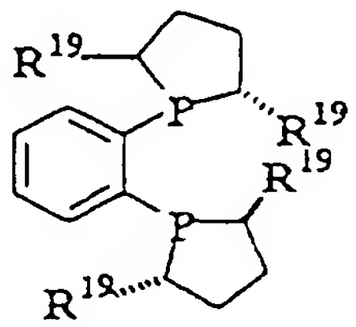
(11)

wherein R^{15} represents a phenyl, 4-methylphenyl, 3-methylphenyl, 3,5-dimethylphenyl, 4-methoxyphenyl, cyclohexyl or cyclopentyl group, R^{16} represents a hydrogen atom, a methyl group or a methoxy group, R^{17} represents a hydrogen atom, a methyl group, a methoxy group or a chlorine atom, and R^{18} represents a methyl, methoxy or trifluoromethyl group. Examples of the optically active tertiary phosphine include (4,4',6,6'-tetramethyl-5,5'-dimethoxybiphenyl-2,2'-diyl)-bis(diphenylphosphine) and, ((4,4',6,6'-tetramethyl-5,5'-dimethoxybiphenyl-2,2'-diyl)-bis(di-p-methoxyphenylphosphine) as described in *Chem. Pharm. Bull.*, 39, 1085(1991); (4,4',6,6'-tetratrifluoromethylbiphenyl-2,2'-diyl)-bis (diphenylphosphine) and (4,6-ditrifluoromethyl-4',6'-dimethyl-5'-methoxybiphenyl-2,2'-diyl)-bis(diphenylphosphine) described in *Synlett*, 827(1991); and 2-dicyclohexyl-2'-diphenylphosphino-4,4',6,6'-tetramethyl-5,5'-dimethoxybiphenyl-2,2'-diyl)-bis(diphenylphosphine) described in *Tetrahedron: Asymmetry*, 3, 13(1992).

[0012] Optically active tertiary phosphines disclosed in JP-B-4-115796 (the term "JP-B" as used herein means an

"examined Japanese patent publication") are also usable. Examples include (6,6'-dimethyl-2,2'-biphenylene)-bis(diphenylphosphine), (4,4',6,6'-tetramethyl-2,2'-biphenylene)-bis(diphenylphosphine), (3,3',6,6'-tetramethyl-2,2'-biphenylene)-bis(diphenylphosphine), (4,4'-difluoro-6,6'-dimethyl-2,2'-biphenylene)-bis(diphenylphosphine), (4,4'-bis(dimethylamino)-6,6'-dimethyl-2,2'-biphenylene)-bis(diphenylphosphine), (6,6'-dimethyl-2,2'-biphenylene)-bis(di-p-tolylphosphine), (6,6'-dimethyl-2,2'-biphenylene)-bis(di-o-tolylphophine), (6,6'-dimethyl-2,2'-biphenylene)-bis(di-m-fluorophenylphosphine), and 1,11-bis(diphenylphosphino)-5,7-dihydrodibenzo[c,e]oxepine. Also usable are those disclosed in JP-A-3-5492 such as (6,6'-dimethoxybiphenyl-2,2'-diyl)-bis(diphenylphosphine), (5,5',6,6'-tetramethoxybiphenyl-2,2'-diyl)-bis(diphenylphosphine), (6,6'-dimethoxybiphenyl-2,2'-diyl)-bis(di-p-tolylphosphine) and (4, 4' , 5, 5', 6, 6' -tetrahexamethoxybiphenyl-2,2'-diyl)-bis(diphenylphosphine).

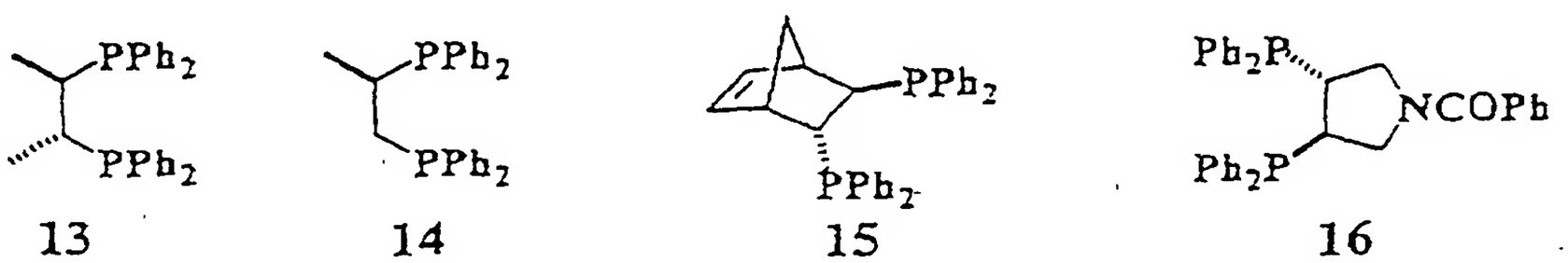
[0013] Examples of the phosphine compound include, in addition to the above-exemplified ones, those represented by the following formula (12):



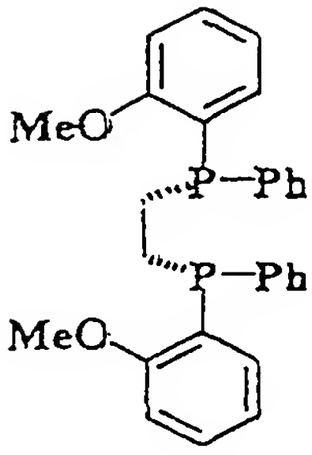
(12)

wherein R^{19} represents a methyl, ethyl, propyl or isopropyl group. Examples of the optically active tertiary phosphine include 1,2-bis(2,5-dimethylphosphorano)benzene, 1,2-bis(2,5-diethylphosphorano)benzene, 1,2-bis(2,5-dipropylphosphorano) benzene and 1,2-bis(2,5-diisopropylphosphorano)benzene as described in *J. Am. Chem. Soc.*, 115, 10125 (1993).

[0014] Examples of the phosphine compound include, in addition to the above-exemplified ones, CHIPAPHOS (2,3-bis-(diphenylphosphino)butane (13), PROPHOS (1,2-bis-(diphenylphosphino)propane) (14), NORPHOS (5,6-bis-(diphenylphosphino)-2-norbornene) (15), DEGPHOS (1-substituted-3,4-bis-(diphenylphosphino)pyrrolidine) (16), BDPP (2,4-bis(diphenylphosphino)pentane) (17), DIOP (2,3-o-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane) (18), DIPAMP (1,2-bis-[(o-methoxyphenyl)phosphino]ethane) (19), BPPHFOH (1-[1'-bis-(diphenylphosphino)ferrocenyl]ethanol) (20), and BPPM (1-tert-butoxycarbonyl-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine (21).



13 14 15 16



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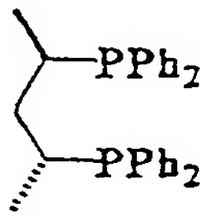

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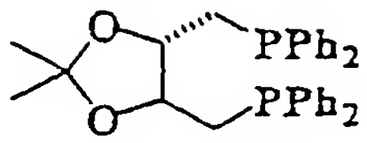

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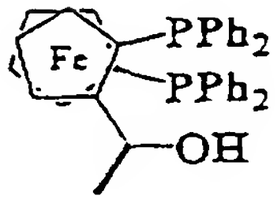

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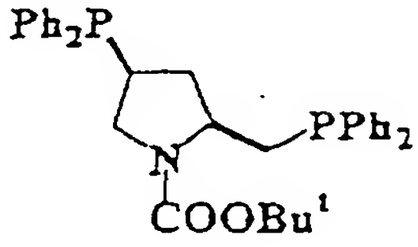
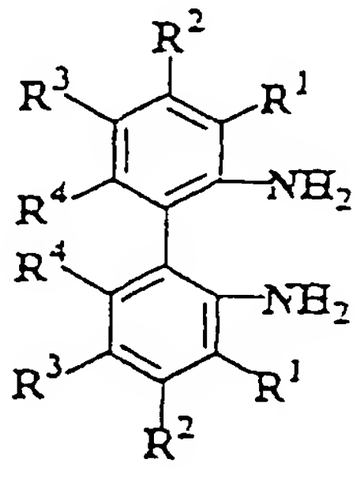


21

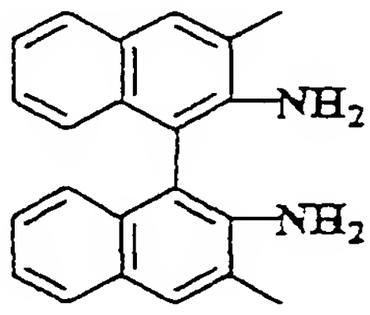
[0015] In the invention, an optically active diamine compound is used as an optically inactivating agent. Examples include optically active chiral diamine compounds each represented by the following formula (4):



(4)

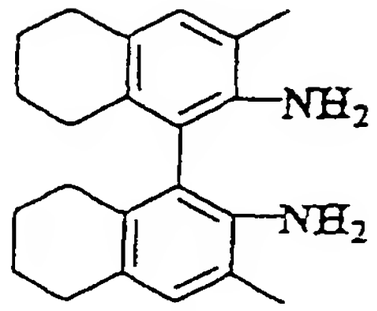
wherein R^1 represents a C_{1-4} lower alkyl group, R^2 represents a hydrogen atom, a methyl group or a methoxy group, R^3 represents a hydrogen atom, a methyl group, a methoxy group or a chlorine atom, R^4 represents a methyl group, a methoxy group or a trifluoromethyl group, or R^3 and R^4 may be coupled together to form a cyclo ring.

[0016] Specific examples include optically active 3,3'-dimethyl-2,2'-diamino-1,1'-binaphthyl of the following formula (22):



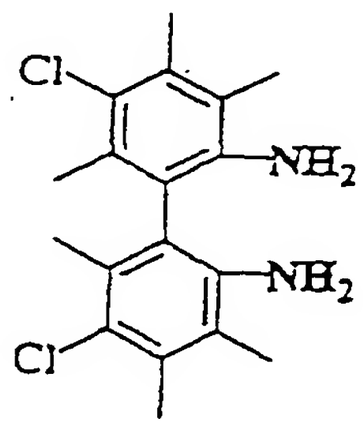
(22)

optically active 3,3'-dimethyl-2,2'-diamino-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl of the following formula (23):



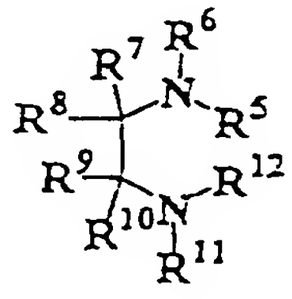
(23)

and optically active 3,3',4,4',6,6'-hexamethyl-2,2'-diamino-1,1'-biphenyl of the following formula (24):



(24)

[0017] In the invention, an optically active amine compound or the like is employed as an optically activating agent. Examples include optically active diamine compounds each represented by the following formula (5):



(5)

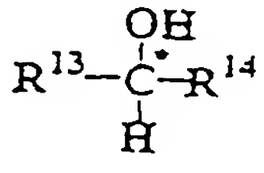
wherein R^5, R^6, R^{11} and R^{12} each independently represents a hydrogen atom, a saturated or unsaturated hydrocarbon group, an aryl group, a urethane group, a sulfonyl group or the like; R^7, R^8, R^9 and R^{10} are the same or different so that the carbon to which these substituents are bonded becomes an asymmetric center and each represents a hydrogen atom, an alkyl group, an aromatic monocyclic or polycyclic group, a saturated or unsaturated hydrocarbon group or a cyclic hydrocarbon group; or R^7 or R^8 and R^9 or R^{10} may be coupled together to form an alicyclic group so that the carbon bonded thereto becomes an asymmetric center.

[0018] Specific examples include optically active diamine compounds such as optically active 1,2-diphenylethylenediamine, 1,2-cyclohexanediamine, 1,2-cycloheptanediamine, 2,3-dimethylbutanediamine, 1-methyl-2,2-diphenylethylenediamine, 1-isobutyl-2,2-diphenylethylenediamine, 1-isopropyl-2,2-diphenylethylenediamine, 1-methyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-isopropyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-isopropyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-benzyl-2,2-di(p-methoxyphenyl)ethylenediamine, 1-methyl-2,9-dinaphthylethylenediamine, 1-isobutyl-2,2-dinaphthylethylenediamine and 1-isopropyl-2,2-dinaphthylethylenediamine and optically active diamine compounds having a sulfonyl or urethane group as one or two of the substituents of R^5 to R^{12}. The diamine compound is used in an amount of 0.5 to 2.5 equivalents, preferably 1 to 2 equivalents relative to the transition metal complex.

[0019] As an organic solvent to be used upon preparation of the complex of the invention, no particular limitation is imposed insofar as it does not react with the ruthenium-phosphine complex easily. Preferred examples include aromatic

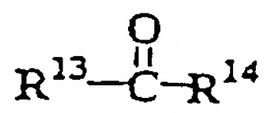
hydrocarbons such as benzene, toluene and xylene, halogenated hydrocarbons such as methylene chloride, chloroform and carbon tetrachloride and aprotic solvents such as tetrahydrofuran, diethyl ether and dimethoxyethane. The reaction temperature can be set within a range of from 0 °C to 30 °C. The reaction time varies, depending on the kind of the organic solvent, ruthenium-phosphine complex, inactivating agent (optically active chiral diamine (4)) or activating agent (optically active diamine derivative (5)) to be employed, but is usually set within a range of from 10 to 180 minutes, preferably 30 to 60 minutes.

[0020] The present invention also provides a process for producing an optically active alcohol represented by the following formula (7):



(7)

wherein * means chiral center, R^{13} represents a substituted or unsubstituted, monocylic or polycyclic aromatic hydrocarbon group or an α,β-unsaturated $C_{2\text{-}10}$ alkyl group and R^{14} represents a substituted or unsubstituted, saturated or unsaturated $C_{1\text{-}10}$ hydrocarbon group or a substituted or unsubstituted monocyclic or polycyclic aromatic hydrocarbon group, or R^{13} and R^{14} may be coupled together to form a saturated or unsaturated alicyclic group which may have a substituent for providing a cyclic ketone, which comprises subjecting, in the presence of an optically active ruthenium-phosphine complex as described above as a catalyst and a base, a ketone compound represented by the following formula (6):



(6)

wherein R^{13} and R^{14} have the same meanings as described above, to asymmetric hydrogenation.

[0021] Examples of the substituted or unsubstituted hydrocarbon group or heterocyclic group represented by R^{13} or R^{14} of the carbonyl compound of the formula (6) employed as a raw material in the process of the invention include substituted or unsubstituted aliphatic hydrocarbon groups, monocylic or polycyclic aromatic hydrocarbon groups, monocyclic or polycyclic alicyclic hydrocarbon groups, and monocyclic or polycyclic heterocylic groups. Among them, as the aliphatic hydrocarbon groups, saturated or unsaturated, linear or branched hydrocarbon groups can be given as examples. Specific examples include alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, hexyl and heptyl and alkenyl groups such as vinyl and allyl. Specific examples of the monocyclic or polycyclic aromatic hydrocarbon group include phenyl, 2-methylphenyl, 2-ethylphenyl, 2-isopropylphenyl, 2-tert-butylphenyl, 2-methoxyphenyl, 2-chlorophenyl, 2-vinylphenyl, 3-methylphenyl, 3-ethylphenyl, 3-isopropylphenyl, 3-methoxyphenyl, 3-chlorophenyl, 3-vinylphenyl, 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl, 4-tert-butylphenyl, 4-vinylphenyl, cumenyl, mesityl, xylyl, 1-naphthyl, 2-naphthyl, anthryl, phenanthryl and indenyl. Specific examples of the monocyclic or polycyclic alicyclic hydrocarbon group include cycloalkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. Specific examples of the monocyclic or polycyclic heterocyclic group include thienyl, furyl, pyranyl, xanthenyl, pyridyl, imidazolinyl, indolyl, carbazoyl and phenanthrolyl. Examples of the substituent for these groups include halogen atoms, hydroxyl group and alkoxyl groups. Also aralkyl groups or ferrocenyl group can be given as the substituent when the above-exemplified hydrocarbon group and heterocyclic group are bonded each other.

[0022] Examples of the aliphatic ring formed by R^{13} and R^{14} together with an adjacent carbon atom include 5 to 12-membered cyclic ketones such as cyclopentanone, cyclohexanone, cycloheptanone, cyclohexenone and cycloheptenone. These cyclic ketones may be substituted with an alkyl, alkenyl, aromatic hydrocarbon, heterocyclic or alkoxyl group.

[0023] As R^{13}, particularly preferred are aliphatic hydrocarbon groups, aromatic hydrocarbon groups and heterocyclic groups, while as R^{14}, aliphatic hydrocarbon groups are preferred, with alkyl groups being particularly preferred. It is also preferred that R^{13} and R^{14} are coupled together with an adjacent carbon atom to form a substituted or unsubstituted cyclic ketone.

[0024] As the base, metal salts each represented by the following formula (25):

MZ (25)

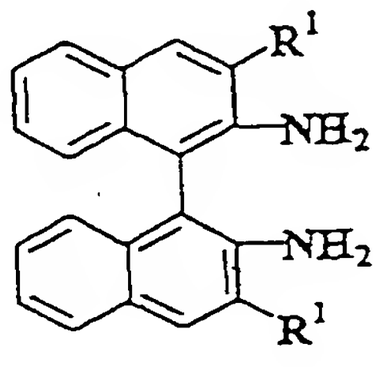
wherein M represents an alkali metal or alkaline earth metal and Z represents a hydroxy, alkoxy, mercapto, naphthyl group or carbonate, or quaternary ammonium salts can be employed. Specific examples include LiOH, LiOMe, LiOEt, $LiOCH(CH_3)_2$, $LiOC(CH_3)_3$, NaOH, NaOMe, NaOEt, $NaOCH(CH_3)_2$, $NaOC(CH_3)_3$, KOH, KOMe, KOEt, $KOCH(CH_3)_2$, $KOC(CH_3)_3$, $KC_{10}H_8$, K_2CO_3 and Na_2CO_3. Quaternary ammonium salts are also usable. The base is used in an amount of 0.5 to 100 equivalents, preferably 2 to 4 equivalents relative to the transition metal complex.

[0025] In the invention, two catalyst components, that is, the optically active ruthenium-phosphine complex of the formula (1) and base, are indispensable for smooth progress of asymmetric hydrogenation reaction and attainment of a high optical yield. An alcohol having a high reaction activity and high optical purity is not available without both components. In the invention, any liquid solvent is usable insofar as it can solubilize reaction raw materials and catalyst system. Examples include aromatic hydrocarbon solvents such as toluene and xylene, aliphatic hydrocarbon solvents such as pentane and hexane, halogen-containing hydrocarbon solvents such as methylene chloride, ether solvents such as ether and tetrahydrofuran, alcohol solvents such as methanol, ethanol, 2-propanol, butanol and benzyl alcohol, and hetero-atom-containing organic solvents such as acetonitrile, DMF and DMSO. The target product is an alcohol so that alcohol solvents are most suited, with 2-propanol being more preferred. When the reaction substrate cannot be solubilized in a solvent easily, a mixture of the solvents selected from the above-exemplified ones can be employed.

[0026] The amount of the solvent is judged from the solubility of the reaction substrate and economy. When 2-propanol is employed, reaction can be effected at a low concentration of 1% or less or in a nearly solventless manner, though depending on the kind of the substrate. Preferred is 20 to 50 % by weight. The hydrogen pressure in the invention is preferably 1 atmospheric pressure because this catalyst system has markedly high activity. In consideration of the economy, however, the hydrogen pressure within a range of 1 to 100 atmospheric pressure is desired, with 3 to 50 atmospheric pressure being more preferred. It is possible to maintain high activity even at a pressure of 10 atmospheric pressure or less when economy of the whole process is taken into consideration.

[0027] Although the reaction is preferably conducted at a temperature within 0 to 140°C, it can be conducted within a range of 30 to 100°C. The reaction time differs with the concentration of the reaction substrate or reaction conditions such as temperature and pressure, but reaction is completed within several minutes to 10 hours. The reaction of the invention can be conducted batchwise or continuously.

[0028] The invention further provides a use of a binaphthyldiamine derivative represented by the following formula (4'):

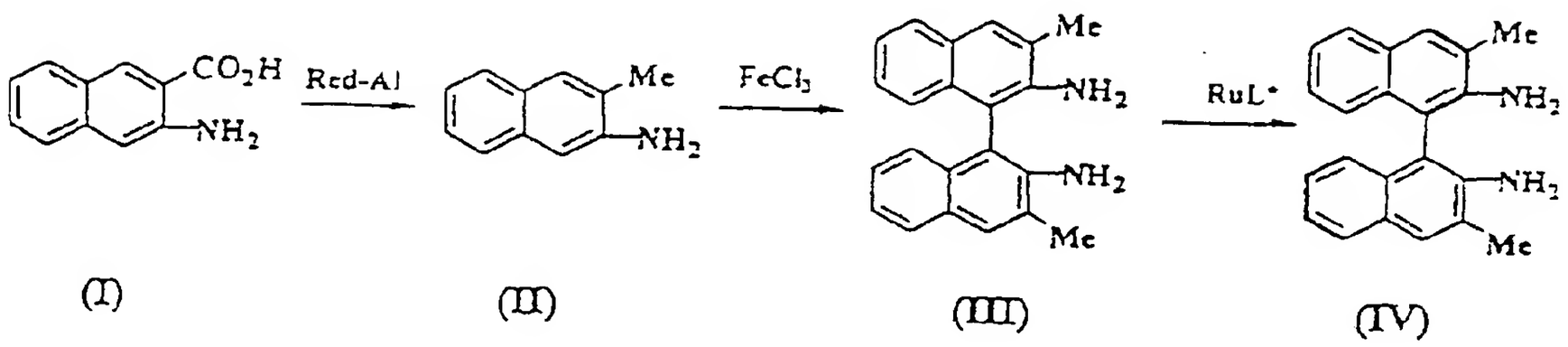


(4')

wherein R^1 represents a C_{1-4} lower alkyl group in the process for producing a mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex of formula (1) .

[0029] In this binaphthyldiamine derivative (4'), specific examples of the C_{1-4} lower alkyl group as R^1 include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl groups.

[0030] The compound (4') of the invention can be prepared in accordance with the below-described reaction scheme. In this reaction scheme (4'), a binaphthyldiamine derivative having as R^1 a methyl group is prepared.



(I) (II) (III) (IV)

[0031] Optically active 3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine (IV) is available by reducing 2-aminonaphthoeic acid (I), which is used as a raw material, with "Red-Al" (trade name, a toluene solution of bis(2-methoxyethoxy)aluminum sodium hydride) to obtain 3-metyl-2-naphthylamine (II), subjecting it to dimerization by using $FeCl_3$ to obtain 3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine (III) and then subjecting it to optical resolution by using optically active RuL* (optically active ruthenium-phosphine complex, for example, $RuCl_2$[binap](dmf) $_n$) .

[0032] The above-described reaction can also be applied to the compound (4') other than that having as R^1 a methyl group.

[0033] The invention compound (4') thus available is useful for inactivating one of the enantiomers of the racemic ruthenium-phosphine complex.

Examples

[0034] The present invention will hereinafter be described in detail by Examples. It should however be borne in mind that the present invention is not limited to or by them.

[0035] Apparatuses employed for measurement of each substance are as follows:

^{1}H Nuclear magnetic resonance spectrum (which will hereinafter be abbreviated as "^{1}H-NMR") :

"GEMINI-300" (300 MHz) (trade name; product of Varian, Inc.)

^{13}C Nuclear magnetic resonance spectrum (which will hereinafter be abbreviated as "^{13}C-NMR") :

"GEMINI-300" (75 MHz) (trade name; product of Varian, Inc.)

Polarimeter: "DIP-140" (trade name; product of JASCO Corporation)
High-performance liquid chromatography (which will hereinafter be abbreviated as "HPLC")
"LC-6A", "SPD-6A" (trade name; product of Shimadzu Corporation)
Gas chromatography (which will hereinafter be abbreviated as "GC")
"Shimadzu GC-14B" (trade name; product of Shimadzu Corporation)
Abbreviations employed in this specification have the following meanings.
(±): racemic form
binap: 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
dm-binap: 2,2'-bis[di(3,5-dimethylphenyl)phosphino]-1,1'-binaphthyl
dmf: dimethylformamide
dpen: 1,2-diphenylethylenediamine

Example 1

Synthesis of 3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine 1) Synthesis of 3-methyl-2-naphthylamine

[0036] Under an argon gas stream, 12.1 g (52 mmol) of 2-aminonaphthoeic acid (80% purity) was dissolved in 350 mL of xylene, followed by the dropwise addition of 117 mL (390 mmol) of Red-Al (trade name; a toluene solution of sodium bis(2-methoxyethoxy)aluminum hydride). After stirring at 150°C for 6 hours, the reaction mixture was cooled and 39 mL (130 mmol) of Red-Al was added dropwise further. After stirring at 150°C for 18 hours, a 20% aqueous KOH solution was added dropwise at 0°C. The reaction mixture was filtered through Celite (trade name) and the filtrate was

washed with a 1N KOH solution. The organic layer was concentrated by distilling off the solvent under reduced pressure. The residue was purified by chromatography on a silica gel column (hexane/ethyl acetate = 4/1 to 3/1), followed by recrystallization from hexane-ethyl acetate, whereby 6.1 g (yield: 75%) of 3-methyl-2-naphthylamine was obtained.
^{1}H NMR($CDCl_3$, 300MHz) 2.36(s,3H), 3.79(br,2H), 7.01(s,1H) 7.22(t,J=7.5Hz, 1H), 7.33(t, J=7.5Hz, 1H), 7.55 (s, 1H) 7.59(d, J=8.1Hz, 1H), 7.65 (d,J=8.1Hz, 1H). ^{13}C NMR($CDCl_3$,75MHz) 17.9, 108.6, 122.4, 125.3, 125.4, 127.0, 128.2, 128.7, 133.7, 143.4, 161.0.

2) Synthesis of 3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine

[0037] At 50°C, 3.1 g (20 mmol) of 3-methyl-2-naphthylamine, 6.5 g (40 mmol) of $FeCl_3$ and 80 mL of H_2O were stirred for 2 hours. To the reaction mixture was added 2 mL of concentrated hydrochloric acid at room temperature. The mixture was stirred at room temperature for 10 minutes. To the reaction mixture were added 20 mL of methylene chloride and 20 mL of a saturated aqueous ammonia solution. After vigorous stirring at room temperature, the reaction mixture was filtered over Celite and the filtrate was washed with methylene chloride. The organic layer was concentrated by distilling off the solvent under reduced pressure. The residue was purified by Florisil (trade name) and then by chromatography on a silica gel column (hexane/ethyl acetate = 4/1 to 3/1). By recrystallization from hexane-chloroform, 0.76 g (yield: 24%) of 3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine was obtained.
^{1}H NMR ($CDCl_3$, 300 MHz) 2.45(s, 6H), 3.45(br, 4H), 7.01(d,J=8.1Hz,2H), 7.15(t, J=7.5Hz, 2H), 7.22(t,J=7.5Hz,2H), 7.70(s,2H), 7.75(d,J=8.1Hz,2H).
^{13}C NMR ($CDCl_3$, 75 MHz) 18.4, 112.8, 122.4, 123.8, 125.2, 125.8, 127.3, 128.4, 128.9, 132.5, 142.1

3) Optical resolution of 3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine

[0038] Under an argon gas, 0.73 g (2.3 mmol) of 3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine and 1.6 g (1.7 mmol) of $RuCl_2$ [(S)-binap](dmf)$_n$ were dissolved in methylene chloride. After stirring at room temperature for 2 hours, the solvent was distilled off under reduced pressure. The residue was purified by chromatography on a neutral silica gel column (methylene chloride), whereby 0.36 g (yield: 49%) of (R)-3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine and 1.2 g (yield: 47%) of an (S)-BINAP-Ru/(S)-diamine complex were obtained. The (R)-3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine was recrystallized in methylene chloride, diethyl ether and hexane, whereby 99%ee of the title compound was obtained.
HPLC analysis of (R)-3HPLC (CHIRALCEL OD-H column, hexane/2-propanol = 80:20, flow rate 0.7 mL/min, detection UV = 254 nm) t_R of R-isomer 12.7 min, t_R of S-isomer 20.3 min.
$[\alpha]_D^{25}$ = +101.5 (c = 0.50, $CHCl_3$)
^{1}H NMR of (S)-BINAP-Ru/(S)-diamine complex
^{1}H NMR (300MHz, $CDCl_3$) δ 1.84(s,6H), 3.95 (d, J=9.6Hz, 2H) 4.70(d,J=8.7Hz,2H), 6.25(d,J=8.7Hz,2H), 6.48(d,J=4.2Hz, 8H), 6.67(t,J=7.2Hz,2H), 6.77(d,J=8.4Hz,2H), 7.02-7.20(m,8H), 7.29-7.39(m,8H), 7.48-7.55(m,4H), 7.69(d,J=16.8Hz, 2H), 7.74(d,J=8.1Hz,2H), 8.01(br,4H), 8.18(m,2H).

Example 2

Asymmetric inactivation and asymmetric activation of racemic DM-BINAP-Ru complex (synthesis of $RuCl_2$[(S)-dm-binap] [(S,S)-dpen]

[0039] Under an argon gas stream, 25 mg (0.05 mmol) of $[RuCl_2(C_6H_6)]_2$, 77 mg (0.11 mmol) of racemic DM-BINAP and 1.8 mL of DMF were charged in a Schlenk tube, followed by stirring at 100°C for 10 minutes. The solvent was then distilled off at 50°C under reduced pressure, whereby 102 mg (yield: 97%) of $RuCl_2$[(±)-dm-binap](dmf)$_n$ was obtained. To the resulting complex were added 16.4 mg (0.053 mmol) of (R)-3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine and 1.8 mL of methylene chloride were added. After stirring for 1 hour, the reaction mixture was cooled to 0°C and 10 mg (0.05 mmol) of (S,S)-1,2-diphenylethylendiamine was added. After stirring at room temperature for 10 minutes, the solvent was distilled off under reduced pressure, whereby a mixture of $RuCl_2$[(S)-dm-binap] [(S, S)-dpen] and $RuCl_2$ [(R) -dm-binap] [(R) -3, 3' - dimethyl-1,1'-binaphthyl-2,2'-diamine] was obtained as a yellow solid (128 mg).

Example 3

Asymmetric hydrogenation reaction of 1'-acetonaphthone

[0040] A 100 mL autoclave was charged with 11.7 mg (0.010 mmol) of the mixture of $RuCl_2$[(S)-dm-binap] [(S,S)-dpen] and $RuCl_2$[(R)-dm-binap] [(R)-3,3'-dimethyl-1,1'-binaphthyl-2,2'-diamine] obtained in Example 2. After purging with argon, 2.8 mL of 2-propanol and 50 μL (0.025 mmol) of KOH/2-propanol (0.5M solution) were added. The resulting mixture

was stirred at room temperature for 30 minutes. After addition of 0.38 mL (2.5 mmol) of 1'-acetonaphthone, stirring was conducted at room temperature for 4 hours at a hydrogen pressure adjusted to 0.8 Mpa. The reaction mixture was concentrated by distilling off the solvent under reduced pressure. The residue was filtered using silica gel, whereby 420 mg (yield: 98.7%) of (R)-1-(1-naphthyl)ethanol was obtained. The enantio-selectivity was 96.2%ee.
$[\alpha]_D^{25}$ = +75.5 (c=1.0, $CHCl_3$)
GC (column, CP-Cyclodextrin-β-2,3,6-M-19, i.d. 0.25 mm x 25 m, CHROMPACK; carrier gas, nitrogen (75 kPa); column temp, 160°C; injection temp, 190°C; split ratio, 1001), t_R of S-isomer 31.6 min, t_R of R-isomer 32.7 min.

Example 4

Synthesis of (R)-1-phenylethanol

[0041] Under similar conditions to those of Example 3 except for the use of acetophenone instead of 1'-acetonaphthone as a raw material, asymmetric hydrogenation was conducted. The conversion ratio was 100%, while the enantio-selectivity was 94.8%ee. GC (column, CP-Cyclodextrin-β-2,3,6-M-19, i.d. 0.25 mm x 25 m, CHROMPACK; carrier gas, nitrogen (75 kPa); column temp, 105°C; injection temp, 135°C; split ratio, 1001), t_R of R-isomer 17.5 min (97.4%), t_R of S-isomer 19.2 min (2.6%).

Example 5

Synthesis of (R)-1-(2-tolyl)ethanol

[0042] Under similar conditions to those of Example 3 except for the use of 2-acetyltoluene instead of 1'-acetonaphthone as a raw material, asymmetric hydrogenation was conducted. The conversion ratio was 100%, while the enantio-selectivity was 95.4%ee. GC (column, CP-Cyclodextrin-β-2,3,6-M-19, i.d. 0.25 mm x 25 m, CHROMPACK; carrier gas, nitrogen (75 kPa); column temp, 130°C; injection temp, 160°C; split ratio, 1001) , t_R of R-isomer 19.2 min (97.7%), t_R of S-isomer 20.4 min (2.3%).

Example 6

Synthesis of (R) -1- (3-tolyl) ethanol

[0043] Under similar conditions to those of Example 3 except for the use of 3-acetyltoluene instead of 1'-acetonaphthone as a raw material, asymmetric hydrogenation was conducted. The conversion ratio was 100%, while the enantio-selectivity was 95.0%ee. GC (column, CP-Cyclodextrin-β-2,3,6-M-19, i.d. 0.25 mm x 25 m, CHROMPACK; carrier gas, nitrogen (75 kPa); column temp, 115°C; injection temp, 145°C; split ratio, 1001), t_R of R-isomer 19.2 min (97.5%), t_R of S-isomer 20.4 min (2.5%).

Example 7

Synthesis of (R)-1-(4-tolyl)ethanol

[0044] Under similar conditions to those of Example 3 except for the use of 4-acetyltoluene instead of 1'-acetonaphthone as a raw material, asymmetric hydrogenation was conducted. The conversion ratio was 100%, while the enantio-selectivity was 93.0%ee. HPLC (CHIRALCEL OB-H column, hexane/2-propanol = 90:10, flow rate 0.5 mL/min, detection UV = 254 nm) t_R of S-isomer 12.4 min (3.5%), t_R of R-isomer 14.6 min (96.5%).

Example 8

Synthesis of (R)-1-(2-naphthyl)ethanol

[0045] Under similar conditions to those of Example 3 except for the use of 2'-acetonaphthone instead of 1'-acetonaphthone as a raw material, asymmetric hydrogenation was conducted. The conversion ratio was 100%, while the enantio-selectivity was 90.6%ee. HPLC (CHIRALPAK AS column, hexane/2-propanol = 98:2, flow rate 1.0 mL/min, detection UV = 254 nm) t_R of R-isomer 14.5 min (95.3%), t_R of S-isomer 16.2 min (4.7%).

Comparative Example 1

[0046] Under an argon gas stream, 25 mg (0.05 mmol) of $[RuCl_2(C_6H_6)]_2$, 68 mg (0.11 mmol) of racemic BINAP and 1.8 mL of DMF were fed to a Schlenk tube, followed by stirring at 100°C for 10 minutes. The solvent was then distilled off at 50°C under reduced pressure, whereby $RuCl_2[(\pm)\text{-binap}](dmf)_n$ was obtained. To the resulting complex were added 15.1 mg (0.053 mmol) of (S)-1,1'-binaphthyl-2,2'-diamine and 1.8 mL of methylene chloride. After stirring for 1 hour, the solvent was distilled off under reduced pressure, whereby a yellow solid was obtained.

[0047] To 100 mL of an autoclave was charged 11.7 mg (0.010 mmol) of the mixture of $RuCl_2[(R)\text{-binap}](dmf)_n$ and $RuCl_2[(S)\text{-binap}]$ [(S)-binaphthyldiamine]. After purging with argon, 2.8 mL of 2-propanol and 50 μL (0.025 mmol) of KOH/2-propanol (0.5M solution) were added. The resulting mixture was stirred at room temperature for 30 minutes. After addition of 0.38 mL (2.5 mmol) of 1'-acetonaphthone, stirring was conducted at room temperature for 4 hours at a hydrogen pressure adjusted to 0.8 Mpa. The reaction mixture was concentrated by distilling off the solvent under reduced pressure. The residue was filtered using silica gel, whereby 228 mg (yield: 53%) of (R)-1-(1-naphthyl)ethanol was obtained. The enantio-selectivity was 4%ee.

Comparative Example 2

[0048] Under an argon gas stream, 25 mg (0.05 mmol) of $[RuCl_2(C_6H_6)]_2$, 68 mg (0.11 mmol) of (S)-BINAP and 1.8 mL of DMF were fed to a Schlenk tube, followed by stirring at 100°C for 10 minutes. The solvent was then distilled off at 50°C under reduced pressure, whereby $RuCl_2[(S)\text{-binap}](dmf)_n$ was obtained. To the resulting complex were added 15.1 mg (0.11 mmol) of (S)-1,1'-binaphthyl-2,2'-diamine and 1.8 mL of methylene chloride were added. After stirring for 1 hour, the solvent was distilled off under reduced pressure, whereby a yellow solid was obtained.

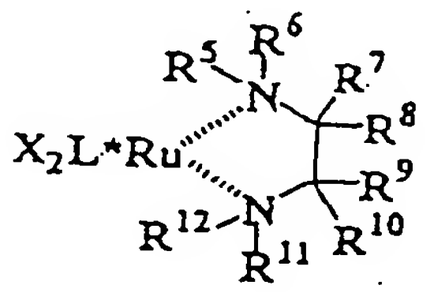
[0049] To 100 mL of an autoclave was fed 11.7 mg (0.010 mmol) of $RuCl_2$ [(S)-binap] [(S)-binaphthyldiamine]. After purging with argon, 2.8 mL of 2-propanol and 50 μL (0.025 mmol) of KOH/2-propanol (0.5M solution) were added. The resulting mixture was stirred at room temperature for 30 minutes. After addition of 0.38 mL (2.5 mmol) of 1'-acetonaphthone, stirring was conducted at room temperature for 4 hours at a hydrogen pressure adjusted to 0.8 Mpa. The reaction mixture was concentrated by distilling off the solvent under reduced pressure. The residue was filtered using silica gel, whereby 202 mg (yield: 47%) of (R)-1-(1-naphthyl)ethanol was obtained. The enantio-selectivity was 30%ee.

[0050] According to the invention, an optically active ruthenium-phosphine complex can be synthesized by reacting a racemic ruthenium phosphine complex with 1/2 equivalent of an optically active chiral inactivating agent and then with an optically active diamine derivative.

[0051] By using the above-described complex, various optically active alcohols are available by an industrially advantageous process at a high purity, high yield and low cost.

Claims

1. A process for producing a mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex represented by the formula (1):



(1)

wherein R^5, R^6, R^{11} and R^{12} each independently represent a hydrogen atom, a saturated or unsaturated hydrocarbon group, an aryl group, a urethane group or a sulfonyl group; R^7, R^8, R^9 and R^{10} are the same or different so that the carbon to which these substituents have been bonded becomes an asymmetric center and each independently represent a hydrogen atom, an alkyl group, an aromatic monocyclic or polycyclic group, a saturated or unsaturated hydrocarbon group or a cyclic hydrocarbon group; or R^7 or R^8, and R^9 or R^{10} may be coupled together to form an alicyclic group so that the carbon bonded thereto becomes an asymmetric center; L represents a bidentate ligand compound of a tertiary phosphine; X represents a halogen atom; and * means chiral center (L* is an optically active substance); said process comprising the steps of:

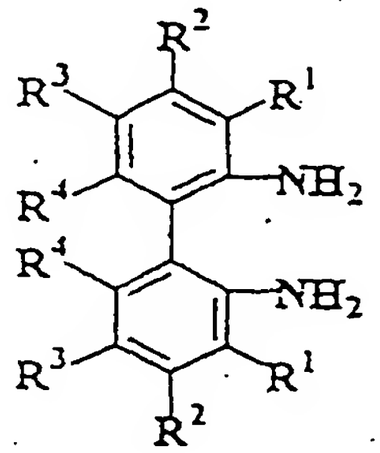
- reacting a ruthenium-phosphine complex represented by the formula (2):

$$Ru_mX_nL_pA_q \qquad (2)$$

wherein X and L have the same meanings as defined above (L is a racemic modification); A represents triethylamine (Et_3N) or dimethylformamide (DMF); and m, n, p and q each stand for an integer and when A represents Et_3N, m, n, p and q stand for 2, 4, 2 and 1, respectively, and when A represents DMF, m, n, p and q stand for 1, 2, 1 and 2 to 5, respectively; or
a ruthenium-phosphine complex represented by the formula (3):

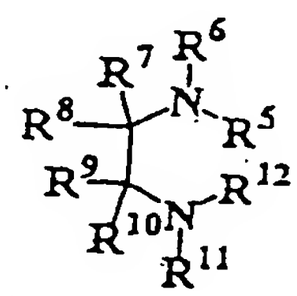
$$[RuX(D)(L)]X \qquad (3)$$

wherein X and L have the same meanings as defined above (L is a racemic modification) and D represents benzene, p-cymene, 1,3,5-trimethylbenzene or hexamethylbenzene;
with 1/2 equivalent of an optically active chiral diamine represented by the formula (4):



(4)

wherein R^1 represents a C_{1-4} lower alkyl group; R^2 represents a hydrogen atom, a methyl group or a methoxy group; R^3 represents a hydrogen atom, a methyl group, a methoxy group or a chlorine atom; R^4 represents a methyl group, a methoxy group or a trifluoromethyl group; or R^3 and R^4 may be coupled together to form a cyclo ring; thereby inactivating only one of the enantiomers;
whereby there are obtained the inactivated enantiomer and the other enantiomer, and then
- reacting said the other enantiomer with an optically active diamine derivative represented by the formula (5):

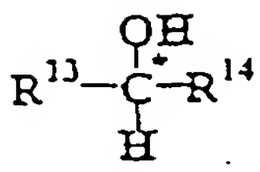


(5)

wherein R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} and R^{12} have the same meanings as defined above;
thereby activating the other enantiomer;
whereby there are obtained the inactivated enantiomer and the activated enantiomer.

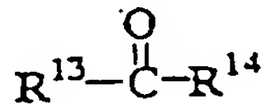
2. A mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex obtainable by the process according to claim 1

3. A process for producing an optically active alcohol represented by the following formula (7):



(7)

wherein * means chiral center, R^{13} represents a substituted or unsubstituted monocylic or polycyclic aromatic hydrocarbon group or an α,β-unsaturated $C_{2\text{-}10}$ alkyl group and R^{14} represents a substituted or unsubstituted saturated or unsaturated $C_{1\text{-}10}$ hydrocarbon group or a substituted or unsubstituted monocyclic or polycyclic aromatic hydrocarbon group, or R^{13} and R^{14} may be coupled together to form a saturated or unsaturated alicyclic group which may have a substituent for providing a cyclic ketone,
which comprises subjecting, in the presence of a mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex as claimed in claim 2 as a catalyst and a base, a ketone compound represented by the following formula (6) to asymmetric hydrogenation:

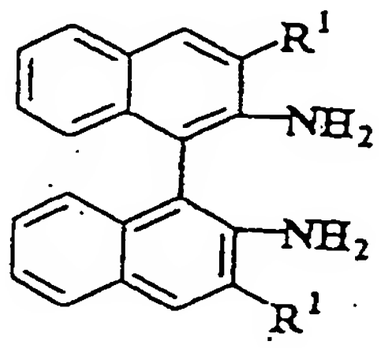


(6)

wherein R^{13} and R^{14} have the same meanings as defined above.

4. The process for producing an optically active alcohol as claimed in claim 3, wherein the base is an alkali metal compound or an alkali earth metal compound.

5. Use of a binaphthyldiamine derivative represented by the formula (4'):

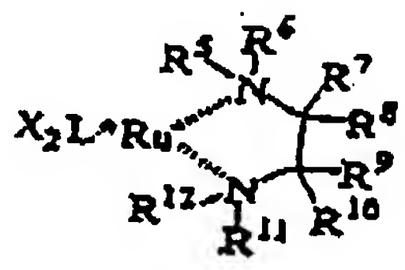


(4')

wherein R^1 represents a $C_{1\text{-}4}$ lower alkyl group;
in the process for producing a mixture of the inactivated enantiomer and activated enantiomer of an optically active ruthenium-phosphine complex according to claim 1.

Patentansprüche

1. Verfahren zum Herstellen eines Gemisches aus dem inaktivierten Enantiomer und aktivierten Enantiomer von einem optisch aktiven Ruthenium-Phosphin-Komplex, der durch die Formel (1) wiedergegeben wird:



(1)

worin R^5, R^6, R^{11} und R^{12} jeweils unabhängig voneinander ein Wasserstoffatom, eine gesättigte oder ungesättigte Kohlenwasserstoffgruppe, eine Arylgruppe, eine Urethangruppe oder eine Sulfonylgruppe bedeuten; R^7, R^8, R^9 und R^{10} gleich oder voneinander verschieden sind, so dass der Kohlenstoff, an welchen diese Substituenten gebunden worden sind, ein asymmetrisches Zentrum wird, und jeweils unabhängig voneinander ein Wasserstoffatom, eine Alkylgruppe, eine aromatische monocyclische oder polycyclische Gruppe, eine gesättigte oder ungesättigte Kohlenwasserstoffgruppe oder eine cyclische Kohlenwasserstoffgruppe bedeuten; oder R^7 oder R^8, und R^9 oder R^{10} miteinander verknüpft sein können unter Bildung einer alicyclischen Gruppe, so dass der daran gebundene Kohlenstoff ein asymmetrisches Zentrum wird; L eine zweizähnige Ligandenverbindung eines tertiären Phosphins bedeutet; X ein Halogenatom bedeutet; und * ein chirales Zentrum bedeutet (L* ist eine optisch aktive Substanz);
wobei das Verfahren die folgenden Schritte umfasst:

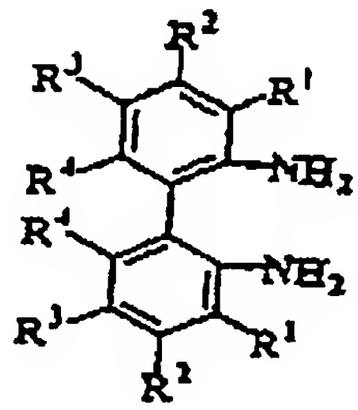
- Umsetzen eines Ruthenium-Phosphin-Komplexes, der durch die Formel (2) wiedergegeben wird:

$$Ru_mX_nL_pA_q \qquad (2)$$

worin X und L die gleichen Bedeutungen wie vorstehend definiert haben (L ist eine racemische Modifikation); A Triethylamin (Et_3N) oder Dimethylformamid (DMF) bedeutet; und m, n, p und q jeweils für eine ganze Zahl stehen und wenn A Et_3N bedeutet, m, n, p und q für 2, 4, 2 bzw. 1 stehen, und wenn A DMF bedeutet, m, n, p und q für 1, 2, 1 bzw. 2 bis 5 stehen; oder
eines Ruthenium-Phosphin-Komplexes, der durch die Formel (3) wiedergegeben wird:

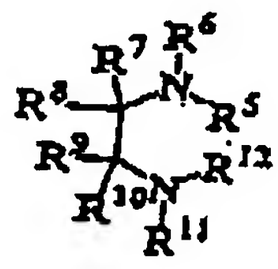
$$[RuX(D)(L)]X \qquad (3)$$

worin X und L die gleichen Bedeutungen wie vorstehend definiert haben (L ist eine racemische Modifikation) und D Benzol, p-Cymol, 1,3,5-Trimethylbenzol oder Hexamethylbenzol bedeutet;
mit ½ Äquivalent von einem optisch aktiven chiralen Diamin, das durch die Formel (4) wiedergegeben wird:



(4)

worin R^1 eine $C_{1\text{-}4}$-Niederalkylgruppe bedeutet; R^2 ein Wasserstoffatom, eine Methylgruppe oder eine Methoxygruppe bedeutet; R^3 ein Wasserstoffatom, eine Methylgruppe, eine Methoxygruppe oder ein Chloratom bedeutet; R^4 eine Methylgruppe, eine Methoxygruppe oder eine Trifluormethylgruppe bedeutet; oder R^3 und R^4 miteinander verknüpft sein können unter Bildung eines Cyclorings;
wodurch nur eines der Enantiomere inaktiviert wird;
wodurch das inaktivierte Enantiomer und das andere Enantiomer erhalten werden, und dann
- Umsetzen des anderen Enantiomers mit einem optisch aktiven Diaminderivat, das durch die Formel (5) wiedergegeben wird:

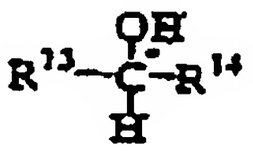


(5)

worin R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} und R^{12} die gleichen Bedeutungen wie vorstehend definiert haben;
wodurch das andere Enantiomer aktiviert wird;
wodurch das inaktivierte Enantiomer und das aktivierte Enantiomer erhalten werden.

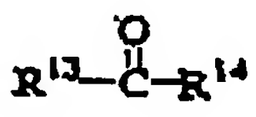
2. Gemisch aus dem inaktivierten Enantiomer und aktivierten Enantiomer von einem optisch aktiven Ruthenium-Phosphin-Komplex, erhältlich durch das Verfahren nach Anspruch 1.

3. Verfahren zum Herstellen eines optisch aktiven Alkohols, der durch die folgende Formel (7) wiedergegeben wird:



(7)

worin * ein chirales Zentrum bedeutet, R^{13} eine substituierte oder unsubstituierte monocyclische oder polycyclische aromatische Kohlenwasserstoffgruppe oder eine α,β-ungesättigte C_{2-10}-Alkylgruppe bedeutet und R^{14} eine substituierte oder unsubstituierte gesättigte oder ungesättigte C_{1-10}-Kohlenwasserstoffgruppe oder eine substituierte oder unsubstituierte monocyclische oder polycyclische aromatische Kohlenwasserstoffgruppe bedeutet oder R^{13} und R^{14} miteinander verknüpft sein können unter Bildung einer gesättigten oder ungesättigten alicyclischen Gruppe, welche einen Substituent aufweisen kann, um ein cyclisches Keton bereitzustellen, welches das Unterwerfen einer Ketonverbindung, die durch die folgende Formel (6) wiedergegeben wird, einer asymmetrischen Hydrierung in Gegenwart eines Gemisches aus dem Inaktivierten Enantiomer und aktivierten Enantiomer von einem optisch aktiven Ruthenium-Phosphin-Komplex wie in Anspruch 2 beansprucht als Katalysator und einer Base umfasst:

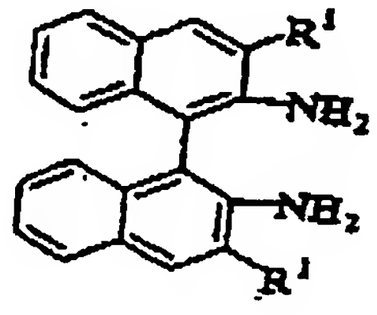


(6)

worin R^{13} und R^{14} die gleichen Bedeutungen wie vorstehend definiert haben.

4. Verfahren zum Herstellen eines optisch aktiven Alkohols wie in Anspruch 3 beansprucht, wobei die Base eine Alkalimetallverbindung oder eine Erdalkalimetallverbindung ist.

5. Verwendung eines Binaphthyldiaminderivats, das durch die Formel (4') wiedergegeben wird:

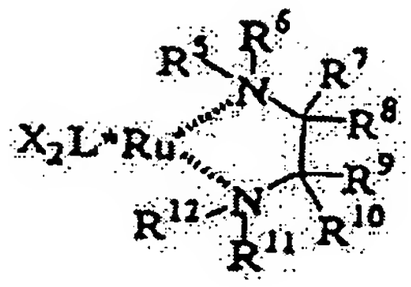


(4')

worin R^1 eine C_{1-4}-Niederalkylgruppe bedeutet;
in dem Verfahren zum Herstellen eines Gemisches aus dem inaktivierten Enantiomer und aktivierten Enantiomer von einem optisch aktiven Ruthenium-Phosphin-Komplex nach Anspruch 1.

Revendications

1. Procédé de préparation d'un mélange de l'énantiomère inactivé et de l'énantiomère activé d'un complexe optiquement actif de ruthénium-phosphine représenté par la formule (1) :



(1)

dans laquelle R^5, R^6, R^{11} et R^{12} représentent chacun indépendamment un atome d'hydrogène, un groupe hydrocarboné saturé ou insaturé, un groupe aryle, un groupe uréthanne ou un groupe sulfonyle ; R^7, R^8, R^9 et R^{10} sont identiques ou différents de façon à ce que l'atome de carbone auquel ces substituants sont liés devienne un centre asymétrique et représentent chacun indépendamment un atome d'hydrogène, un groupe alkyle, un groupe monocyclique ou polycyclique aromatique, un groupe hydrocarboné saturé ou insaturé ou un groupe hydrocarboné cyclique ; ou R^7 ou R^8, et R^9 ou R^{10} peuvent être couplés ensemble pour former un groupe alicyclique de façon à ce que l'atome de carbone lié à ceux-ci devienne un centre asymétrique ; L représente un composé de ligand bicoordiné d'une phosphine tertiaire ; X représente un atome d'halogène ; et * signifie un centre chiral (L* est une substance optiquement active) ; ledit procédé comprenant les étapes consistant à :

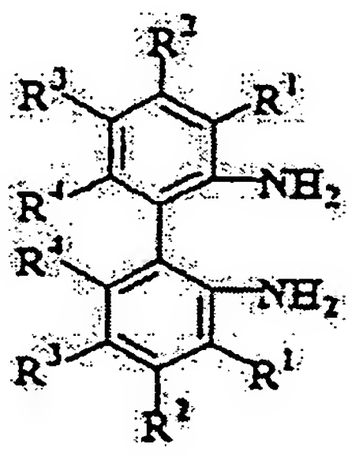
- faire réagir un complexe de ruthénium-phosphine représenté par la formule (2) :

$$Ru_mX_nL_pA_q \qquad (2)$$

dans laquelle X et L ont les mêmes significations que celles définies ci-dessus (L est une modification racémique) ; A représente la triéthylamine (Et_3N) ou le diméthylformamide (DMF) ; et m, n, p et q représentent chacun un nombre entier, et quand A représente Et_3N, m, n, p et q représentent respectivement 2, 4, 2 et 1, et quand A représente le DMF, m, n, p et q représentent respectivement 1, 2, 1 et 2 à 5 ; ou
un complexe de ruthénium-phosphine représenté par la formule (3) :

$$[RuX(D)(L)]X \qquad (3)$$

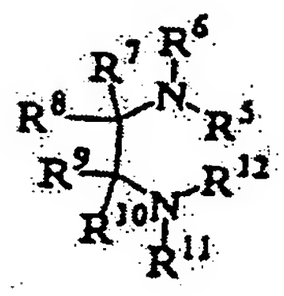
dans laquelle X et L ont les mêmes significations que celles définies ci-dessus (L est une modification racémique) et D représente le benzène, le p-cymène, le 1,3,5-triméthylbenzène ou l'hexaméthylbenzène ;
avec ½ équivalent d'une diamine chirale optiquement active représentée par la formule (4) :



(4)

dans laquelle R^1 représente un groupe alkyle inférieur en C_1 à C_4 ; R^2 représente un atome d'hydrogène, un groupe méthyle ou un groupe méthoxy ; R^3 représente un atome d'hydrogène, un groupe méthyle, un groupe méthoxy ou un atome de chlore ; R^4 représente un groupe méthyle, un groupe méthoxy ou un groupe trifluorométhyle ; ou R^3 et R^4 peuvent être couplés ensemble pour former un noyau cyclo ; inactivant ainsi seulement l'un des énantiomères ; moyennant quoi on obtient l'énantiomère inactivé et l'autre énantiomère, et ensuite

- faire réagir ledit autre énantiomère avec un dérivé de diamine optiquement active représenté par la formule (5) :



(5)

dans laquelle R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} et R^{12} ont les mêmes significations que celles définies ci-dessus ;
activant ainsi l'autre énantiomère ;
moyennant quoi on obtient l'énantiomère inactivé et l'énantiomère activé.

2. Mélange de l'énantiomère inactivé et de l'énantiomère activé d'un complexe optiquement actif de ruthénium-phosphine pouvant être obtenu au moyen du procédé selon la revendication 1.

3. Procédé de préparation d'un alcool optiquement actif représenté par la formule (7) suivante :

(7)

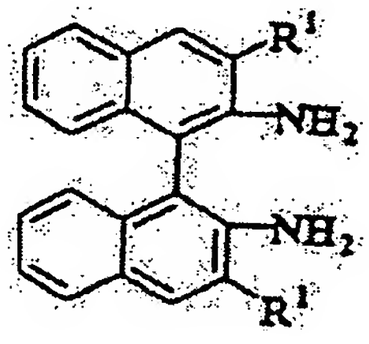
dans laquelle * signifie un centre chiral, R^{13} représente un groupe hydrocarboné aromatique monocyclique ou polycyclique substitué ou non substitué ou un groupe alkyle α, β-insaturé en C_2 à C_{10} et R^{14} représente un groupe hydrocarboné en C_1 à C_{10} saturé ou non saturé, substitué ou non substitué, ou un groupe hydrocarboné aromatique monocyclique ou polycyclique substitué ou non substitué, ou R^{13} et R^{14} peuvent être couplés ensemble pour former un groupe alicyclique saturé ou insaturé qui peut avoir un substituant pour fournir une cétone cyclique,
comprenant l'étape consistant à soumettre, en présence d'un mélange de l'énantiomère inactivé et de l'énantiomère activé d'un complexe optiquement actif de ruthénium-phosphine selon la revendication 2 en tant que catalyseur et d'une base, un composé cétone représenté par la formule (6) suivante à une hydrogénation asymétrique :

(6)

dans laquelle R^{13} et R^{14} ont les mêmes significations que celles définies ci-dessus.

4. Procédé de préparation d'un alcool optiquement actif selon la revendication 3, dans lequel la base est un composé de métal alcalin ou un composé de métal alcalino-terreux.

5. Utilisation d'un dérivé de binaphtyldiamine représenté par la formule (4') :



(4')

dans laquelle R^1 représente un groupe alkyle inférieur en C_1 à C_4 ;

dans le procédé de préparation d'un mélange de l'énantiomère inactivé et de l'énantiomère activé d'un complexe optiquement actif de ruthénium-phosphine selon la revendication 1.